

Notice of Allowability

Application No.

09/341,700

Examiner

Jane Zara

Applicant(s)

SCHLINGENSIEPEN ET AL.

Art Unit

1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 3-18-04.
2. ☒ The allowed claim(s) is/are 70-78.
3. ☐ The drawings filed on _____ are accepted by the Examiner.
4. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) ☒ All b) ☐ Some* c) ☐ None of the:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
6. ☒ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
 - (a) ☒ including changes required by the Notice of Draftperson's Patent Drawing Review (PTO-948) attached
 - 1) ☒ hereto or 2) ☐ to Paper No./Mail Date _____.
 - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with William Player on or about 5-10-04.

The application has been amended as follows:

Please replace claim 70 with the following:

Claim ~~70~~¹ (amended) A method for the selection and preparation of an effective antisense oligonucleotide for a nucleic acid comprising the steps of

designing an antisense oligonucleotide corresponding to a target nucleic acid sequence, such that

- a) the antisense oligonucleotide comprises at least 8 nucleic acid residues,
- b) the antisense oligonucleotide comprises a maximum of twelve elements, each the twelve elements being a nucleotide capable of forming three hydrogen bonds to a cytosine base,
- c) the antisense oligonucleotide does not contain four or more consecutive elements,

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d) the antisense oligonucleotide does not contain two or more series of three consecutive elements, and

e) the ratio of residues forming two hydrogen bonds each with the target nucleic acid sequence with respect to residues forming three hydrogen bonds each with the target nucleic acid sequence is

$$\frac{3\text{H-bond-R}}{3\text{H-bond-R} + 2\text{H-bond-R}} \geq 0.29$$

wherein

- 3H-bond-R = residues forming three hydrogen bonds per residue and
 - 2H-bond-R = residues forming two hydrogen bonds per residue,
- generating the designed antisense oligonucleotide, and
- synthesizing the generated antisense oligonucleotide.

In claim 75, line 5, a comma (--,--) has been inserted after "sugar".

Please replace claim 78 with the following:

⁹
Claim ~~78~~ (amended) An antisense oligonucleotide consisting of SEQ ID NO:
1754.

Examiner's Reasons for Allowance

The following is an examiner's statement of reasons for allowance: The claimed invention is free of the prior art of record because the prior art of record does not teach or fairly suggest a method of selecting antisense oligonucleotides comprising designing an antisense that comprises a maximum of twelve elements (which elements are nucleotides capable of forming three hydrogen bonds each with a cytosine base), but which antisense does not contain four or more consecutive elements, nor two or more series of three consecutive elements, and the ratio of residues forming two hydrogen bonds each with the target nucleic acid target nucleic acid sequence $3H\text{-bond-R}/(3H\text{-bond-R} + 2H\text{-bond-R})$ is greater than or equal to 0.29, and preferably between 0.33 and 0.86. The instant invention is free of the prior art of Stull, James and Probst because the instant invention teaches a method to facilitating optimal selection of antisense oligonucleotide targets by using thermodynamic indices to calculate the free energy of secondary structure (Sscore), while taking into consideration the local mRNA secondary structures at the target site, and free energy estimations of the duplex score (Dscore) and determining the differences between the Dscore and the Sscore (e.g. Cscore).


Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is **703-872-9306**. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(571) 272-0765**. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (571) 272-0760. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (571) 272-0564. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

JZ
5-10-04



RAM R. SHUKLA, PH.D.
PRIMARY EXAMINER